

# Prior History of Falls and Risk of Outcomes in Atrial Fibrillation

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# Accepted Manuscript

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**Prior history of falls and risk of outcomes in atrial fibrillation:  
The Loire Valley Atrial Fibrillation Project**

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All authors had access to the data and a role in writing the manuscript

**Running heading:** Falls and risk of outcomes in atrial fibrillation

## Abstract

*Background and Purpose* Patients with non-valvular atrial fibrillation are often denied oral anticoagulation due to falls risk. The latter is variably defined and existing studies have not compared the associated risk of bleeding with other cardiovascular events. There are no data regarding outcomes in individuals with non-valvular atrial fibrillation with a prior history of (actual) falls, rather than being ‘at risk of falls’. Our objective was to evaluate the risk of cardiovascular outcomes associated with prior history of falls in patients with atrial fibrillation in a contemporary ‘real world’ cohort.

*Methods* Patients with non-valvular atrial fibrillation in a four-hospital-institution between 2000 and 2010 were included. Stroke/thromboembolism event rates were calculated according to prior history of falls. Risk factors were investigated by Cox regression.

*Results* Among 7156 atrial fibrillation patients, prior history of falls/trauma was uncommon (n=76; 1.1%) and compared with patients without history of falls, those patients were older, less likely to be on oral anticoagulation and had higher risk scores for stroke/thromboembolism, but not for bleeding.

Compared with no prior history of falls, rates of stroke/thromboembolism ( $p=0.01$ ) and all-cause mortality ( $p<0.0001$ ) were significantly higher in patients with previous falls.

In multivariable analyses, prior history of falls was independently associated with stroke/thromboembolism (hazard ratio, HR 5.19, 95% CI 2.1-12.6;  $p<0.0001$ ), major bleeding (HR 4.01, 1.49-10.8;  $p=0.006$ ) and all-cause mortality (HR 3.69, 1.52-8.95;  $p=0.04$ ), but not haemorrhagic stroke (HR 4.20, 0.58-30.48;  $p=0.16$ ) in patients on oral anticoagulation.

*Conclusion* In this large ‘real world’ atrial fibrillation cohort, prior history of falls was uncommon, but independently increased risk of stroke/thromboembolism, bleeding and mortality, but not haemorrhagic stroke in the presence of anticoagulation. Prior history of (actual) falls may be a more clinically useful risk prognosticator than “being at risk of falls”.

**Key words:** atrial fibrillation; falls; stroke; thromboembolism; bleeding

**Abbreviations and Acronyms**

CHADS <sub>2</sub>	Acronym for Congestive heart failure, Hypertension, Age $\geq 75$ years, Diabetes, previous Stroke
CHA <sub>2</sub> DS <sub>2</sub> -VASc	Acronym for Congestive heart failure, Hypertension, Age $\geq 75$ years, Diabetes, previous Stroke, Vascular disease, Age 65-74 years, Sex category (female)
HAS-BLED	Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly ( $> 65$ years), Drugs/alcohol concomitantly
VKA	Vitamin K antagonist
NOAC	Non-VKA Oral Anticoagulants (previously referred to as new or novel oral anticoagulants)

## Introduction

The global burden of non-valvular atrial fibrillation and ischaemic stroke/thromboembolism is unquestionable(1-3). Oral anticoagulation, most commonly with the vitamin K antagonists (VKA, e.g. warfarin), but also with non-VKA oral anticoagulants (NOACs)(4,5), confers a well-established prognostic benefit for prevention of ischaemic stroke/thromboembolism in the setting of atrial fibrillation.

All oral anticoagulants also confer a risk of bleeding(6), but even in patients with high levels of comorbidity, the net clinical benefit is still in favour of oral anticoagulation(7,8), and the same is probably true for NOACs(5). Therefore, oral anticoagulation is recommended in all individuals with atrial fibrillation other than those who are at truly low-risk of ischaemic stroke/thromboembolism(9). However, despite improved clinical risk prediction tools for risk stratification of ischaemic stroke/thromboembolism and bleeding and consensus guideline recommendations(10,11), levels of oral anticoagulation are still suboptimal in clinical practice, especially in the elderly(12).

One of the commonest reasons for not giving oral anticoagulation is a perceived risk of falls(13-17). Falls are a significant cause of morbidity and mortality, particularly in older populations, and incur high costs to individuals and health systems(18). Of note, the aetiology of falls is multi-factorial(19,20). AF itself is an independent predictor of falls(21,22). In the setting of atrial fibrillation, the main focus of the physician's concern regarding falls is the increased predisposition to major bleeding if oral anticoagulation is initiated(14,15). However, patients on oral anticoagulation at high risk of falls do not necessarily have a significantly increased risk of major bleeds(23), suggesting that being at risk of falls is not a contraindication to oral anticoagulation. Even studies which have shown a high rate of intracranial haemorrhage in atrial fibrillation patients with high risk of falls suggest that there is still an overall benefit of oral anticoagulation due to prevention of ischaemic stroke(24).

Some studies have considered patients with AF at increased risk of falls but with varying definitions and in different subpopulations(21-27). A previous history of (actual) falls is probably the strongest risk factor for future falls, but the risk of cardiovascular events associated with previous history of falls has not been compared with risk of major bleeding in atrial fibrillation patients.

In the first contemporary study of its kind, our objective was to evaluate the risk of bleeding and cardiovascular outcomes associated with a prior history of (actual) falls - rather than 'being at risk of falls' per se - in a large, "real- world" cohort of individuals with atrial fibrillation. We tested the hypothesis that prior history of falls would have an impact on ischaemic stroke/thromboembolism, bleeding and mortality in patients with atrial fibrillation.

## Methods

### *Study population*

The methods of the Loire Valley Atrial Fibrillation Project, which is based at the Centre Hospitalier Régional et Universitaire in Tours (France), have been previously reported<sup>(28)</sup>. The institution includes four hospitals covering all medical and surgical specialties, and is the only public institution in an area of around 4,000 km<sup>2</sup>, serving approximately 400,000 inhabitants. All patients diagnosed with atrial fibrillation or atrial flutter by the cardiology department between 2000-2010 were identified<sup>(28)</sup>, excluding patients with valvular atrial fibrillation. Patients were followed from the first record of atrial fibrillation after 1 January 2000 (i.e. index date) up to the latest data collection at the time of study (December 2010). Treatment at discharge was obtained by screening hospitalisation reports, and information on comorbidities was obtained from the computerised coding system.

Prior history of falls was ascertained from clinical history or medical records. For each patient, the CHADS<sub>2</sub>(10) and CHA<sub>2</sub>DS<sub>2</sub>-VASc(11) scores were calculated. The CHADS<sub>2</sub> score was the sum of points obtained after adding one point for congestive heart failure, hypertension, age  $\geq 75$ , and diabetes, and two points for previous stroke or thromboembolism(11). The CHA<sub>2</sub>DS<sub>2</sub>-VASc score was the sum of points after adding one point for congestive heart failure, hypertension, diabetes, vascular disease (including history of coronary, cerebrovascular or peripheral vascular disease), age 65-74, and female gender, and two points for previous stroke or thromboembolism and age  $\geq 75$ (11). According to the two risk scores, patients with a score of 0 on either schema were considered as 'low risk', 1 as 'intermediate risk', and  $\geq 2$  as 'high risk' of stroke and thromboembolism.

The HAS-BLED (Hypertension, Abnormal renal and/or liver function, Stroke, Bleeding history or predisposition, Labile International Normalized Ratio (INR), Elderly (> 65 years), Drugs (antiplatelet drugs or NSAIDs)/alcohol excess concomitantly) score is a validated scoring system for bleeding risk stratification in AF patients(29). For each patient, the HAS-BLED score was also calculated as the sum of the points obtained after adding one point for the presence of each individual factor). Patients with HAS-BLED score of 0-2 were deemed to have 'low' bleeding risk and those with HAS-BLED score of  $\geq 3$  were classified as 'high' bleeding risk.



During follow-up, information on outcomes of thromboembolism, stroke (ischaemic or haemorrhagic), major bleeding, and all-cause mortality were recorded. Major bleeding was defined as bleeding with a reduction in the haemoglobin level of at least 2g per litre, or with transfusion of at least 1 unit of blood, or symptomatic bleeding in a critical area or organ (e.g., intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome) or bleeding that causes death. All bleeding data were identified with the diagnosis coded in a subsequent hospitalization during follow-up – thus, we recorded all 'hospitalizations with a bleed' as an additional criterion for major bleeding.

### *Statistical analysis*

Risk factors were investigated by Cox regression. Baseline characteristics were determined based on prior history of falls and differences were investigated using chi-squared test for categorical covariates and Kruskal-Wallis test for continuous covariates.

Event rates of ischaemic stroke/thromboembolism, bleeding and all-cause mortality were calculated for all patients by prior history of falls, stratifying by presence or absence of VKA therapy. Haemorrhagic strokes were excluded from analyses of “ischaemic stroke” or “ischaemic stroke/thromboembolism”. Event rates were also calculated by age and sex categories. The risk associated with prior history of falls was estimated in Cox proportional-hazard models. Both univariate and multivariate (including all the CHA<sub>2</sub>DS<sub>2</sub>-VASc risk factors) Cox regression models were applied. A two-sided p-value <0.05 was considered statistically significant. All analyses were performed with SPSS statistical software version 18.0 (IBM, USA).

### *Ethics approval*

The study was approved by the local ethical board of our institution (Pôle Cœur Thorax Vasculaire, Centre Hospitalier Universitaire Trousseau, Tours, France). The informed consent of patients was deemed unnecessary for our analyses since this is a retrospective analysis of a single centre cardiology department.

## Results

From the whole cohort, 7156 patients with nonvalvular atrial fibrillation were included in the analyses. Baseline characteristics are displayed in Table 1. Prior history of falls was uncommon (76/7156=1.1%). Patients with prior history of falls were older ( $p<0.0001$ ), and after age-adjustment, were more likely to be diabetic ( $p=0.009$ ), have coronary artery disease ( $p=0.04$ ) and take ACE-inhibitors ( $p=0.04$ ) and anti-arrhythmic agents ( $p=0.03$ ). Patients with prior history of falls were less likely to take vitamin K antagonists ( $p<0.0001$ ) and antithrombotic agents ( $p=0.002$ ) and had higher CHADS<sub>2</sub> ( $p=0.001$ ) and CHA<sub>2</sub>DS<sub>2</sub>VASc scores ( $p=0.02$ ). HAS-BLED scores did not significantly differ by history of falls ( $p=0.19$ ).

Of the cohort, 3607/7156 (50.4%) of all patients but only 24.3% (17/76) of patients with prior history of falls were on VKA. Event rates for ischaemic stroke ( $p=0.01$ ), ischaemic stroke/thromboembolism ( $p=0.01$ ) and all-cause mortality ( $p<0.0001$ ) were significantly higher in patients with prior history of falls, but not rates of bleeding ( $p=0.38$ ) and haemorrhagic stroke ( $p=0.09$ ) (Table 2). In individuals with history of falls, the event rates per 100 person-years were 1.18 (0.54,2.25) for ischaemic stroke, 1.58(0.82,2.76) for ischaemic stroke/thromboembolism, 0.39(0.08,1.15) for haemorrhagic stroke, 1.05(0.45,2.07) for bleeding and 2.63(1.61,4.06) for all-cause mortality.

### *Sensitivity analysis*

Regardless of history of falls, there were no significant differences between anticoagulated and non-anticoagulated individuals for event rates for ischaemic stroke, ischaemic stroke/thromboembolism, all-cause mortality, bleeding or haemorrhagic stroke (Table 3).

### *Multivariable analysis*

Cox regression analyses for all AF patients with HF are presented in Table 4. On univariable analyses in patients overall, prior history of falls significantly increased the risk of ischaemic stroke/thromboembolism (hazard ratio, HR 2.75, 1.55-4.88;  $p=0.001$ ), haemorrhagic stroke (HR 3.79, 1.20-12.00;  $p=0.02$ ), bleeding (HR 1.86, 1.08-3.23;  $p=0.026$ ) and all-cause mortality (HR 2.74, 1.75-4.27;  $p<0.0001$ ). On multivariable analysis, only the associations for ischaemic stroke/thromboembolism (HR 1.71, 1.04-2.83;  $p=0.04$ ) and all-cause mortality (HR 1.68, 1.07-2.62;  $p=0.02$ ) remained significant.

In anticoagulated individuals, prior history of falls was associated with increased risk of ischaemic stroke/thromboembolism (HR 5.18, 2.13-12.61;  $p<0.0001$ ), bleeding (HR 3.70, 1.38-9.97;  $p=0.01$ ) and all-cause mortality (HR 3.91, 1.61-9.51;  $p=0.003$ ) in multivariate analyses, but not haemorrhagic stroke (HR 4.36, 0.60-31.83;  $p=0.15$ ). In non-anticoagulated individuals, there was no independent association between prior history of falls and ischaemic stroke/thromboembolism, bleeding, haemorrhagic stroke or all-cause mortality.

## Discussion

In the first study of bleeding and cardiovascular outcomes in patients with history of falls and in this large 'real world' atrial fibrillation cohort, our principal findings are as follows: (i) prior history of falls was uncommon, but independently increased risk of ischaemic stroke/thromboembolism by five-fold, and of bleeding and mortality by nearly four-fold, in the presence of anticoagulation; and (ii) the risk of haemorrhagic stroke was not increased in anticoagulated individuals.

In a US cohort of Medicare-treated individuals(24), 1245/18261 (6.8%) were at high risk of falls, compared to the 1.1% of our study population with prior history of falls. The rate of intracranial haemorrhage per 100 patient-years in that study was 2.8 (1.9-4.1) in patients at high risk for falls and 1.1 (1.0-1.3) in other patients(24). In another US study of patients on anticoagulation for any indication, the incidence per 100 patient-years of major bleeding was 8.0 in patients at high risk of falls versus 6.8 in those at low risk of falls(23). Interestingly, the incidence of major bleeding directly after a fall was only 0.6 per 100 patient-years. We observed lower event rates in our population.

The increased risk of ischaemic stroke/thromboembolism and all-cause mortality in anticoagulated patients with history of falls probably reflects increased comorbidities and higher baseline risk stratification scores (e.g. CHA<sub>2</sub>DS<sub>2</sub>-VASc), compared with patients with no history of falls, rather than any association between falls and ischaemic stroke/thromboembolism per se. In individuals not on anticoagulation, there was no independent association between history of falls and ischaemic stroke/thromboembolism, bleeding (including haemorrhagic stroke) or mortality, suggesting that other comorbidities were more important in influencing outcomes (i.e. CHA<sub>2</sub>DS<sub>2</sub>-VASc risk factors).

In our study population, only 24.3% of patients with history of falls were on VKA therapy, compared with 55.9% of patients without history of falls. This proportion of anticoagulated individuals is much lower than other studies<sup>(24,25)</sup>, but is consistent with the well-documented reluctance of healthcare professionals to prescribe VKA in the context of risk of falls<sup>(14-16)</sup>. Surprisingly, in our study population, there was no statistically significant difference in event

rates for ischaemic stroke/thromboembolism or mortality between anticoagulated and non-anticoagulated individuals, regardless of history of falls.

Although history of falls increased the risk of major bleeding in anticoagulated individuals, there was no associated increased risk of haemorrhagic stroke. This is consistent with a Markov decision analysis, which estimated that individuals taking warfarin must fall 295 times in one year in order for the benefits of warfarin therapy to be outweighed by the risk of intracranial haemorrhage(26).

#### *Study limitations.*

This study is based on a ‘real world’ registry with inherent limitations of diagnostic coding and case ascertainment, as previously reported(28). Despite stratification and adjustment for several risk factors, the non-randomized design leaves a risk of residual confounding factors. If a resident moved away from the area or died or had a stroke diagnosed elsewhere, information on the event was not available. However, the relatively high number of deaths in our study suggests a high proportion of ascertainment of events. The study population was hospital-based and therefore may not be representative of all patients with AF, many of whom are not hospitalized for their arrhythmia. The study was not ethnically diverse and our findings may not be generalisable to other populations.

The data regarding oral anticoagulation use are only regarding baseline therapy and do not reflect any changes in prescribed therapy or adherence to therapy. Also, data regarding the “time in therapeutic range” are not available for our study population. Our study population was a prospective cohort design and not a randomised clinical trial, therefore, confounding by indication is a possibility(30). However, the effect of this confounding is likely to be minimal since the individuals at highest risk of study outcomes (based on risk prediction scores) were least likely to be taking oral anticoagulation.

#### *Conclusions*

In this large ‘real world’ atrial fibrillation cohort, prior history of falls was uncommon, but independently increased risk of ischaemic stroke/thromboembolism, bleeding and mortality, but not haemorrhagic stroke in the presence of anticoagulation. Prior history of (actual) falls may be a more clinically useful risk prognosticator than “being at risk of falls” per se.

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LF, NC and KH made the primary contribution to data collection. AB, GYHL, and LF contributed to the study conception and design. AB performed the analyses and produced the initial manuscript. All authors contributed to interpretation of results, revising the manuscript critically for important intellectual content, and all approved the final manuscript. AB, LF and GYHL had full access to all the data in the study and AB takes responsibility for the integrity of the data and the accuracy of the data analysis.

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## Disclosures

Prof Lip has served as a consultant for Bayer, Astellas, Merck, AstraZeneca, Sanofi Aventis, Biotronik, BMS/Pfizer, and Boehringer Ingelheim and has been on the speakers bureau for Bayer, BMS/Pfizer, Boehringer Ingelheim, and Sanofi Aventis. Dr Fauchier has served as a consultant for Bayer, Medtronic and Sanofi Aventis and has received funding for conference travel and educational symposia from Boehringer Ingelheim, Bayer, Medtronic, and Sanofi Aventis. Dr Banerjee reports no conflicts of interest.

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**Table 1: Characteristics of patients with atrial fibrillation by risk of falls**

n (%)	Prior history of falls n=76	No history of falls n=7080	p-value	Age-adjusted p-value
Mean age (SD)	82.9(8.9)	69.9(15.1)	<0.0001	
Female	43(56.6)	2661(37.6)	0.001	0.23
Type of AF				
Paroxysmal	48(63.2)	4128(58.3)	0.49	0.57
Permanent	26(34.2)	2578(36.4)		
Persistent	2(2.6)	374(5.3)		
Comorbidities				
Hypertension	40(52.6)	2992(42.3)	0.05	0.41
Diabetes	19(25.0)	1089(15.4)	0.02	0.009
Previous stroke	12(15.8)	582(8.2)	0.03	0.08
Coronary artery disease	17(22.4)	2113(29.8)	0.17	0.04
Any vascular disease	21(27.6)	2339(33.0)	0.19	0.08
Heart failure	24(31.6)	3502(49.5)	0.002	0.11
Renal impairment	12(15.8)	540(7.6)	0.02	0.13
Liver impairment	0(0)	19(0.3)	0.82	0.99
Dyslipidaemia	11(14.5)	1352(19.1)	0.19	0.90
Smoking	5(6.6)	912(12.9)	0.06	0.49
Pacemaker/ICD	13(17.1)	1141(16.1)	0.76	0.60
Bleeding risk factors				
Previous bleeding	6(7.9)	323(4.6)	0.16	0.39
Labile INR	3(3.9)	119(1.7)	0.14	0.10
Anaemia	0(0)	41(0.6)	0.65	0.98
NSAIDs	1(1.3)	9(0.1)	0.10	0.10
Drugs	10(13.2)	1225(17.3)	0.45	0.13
Cancer (active)	0(0)	119(1.7)	0.64	0.99
Thrombocytopenia	0(0)	6(0.1)	0.94	0.99
Antithrombotic agents				
Vitamin K antagonist	17(24.3)	3590(55.9)	<0.001	<0.0001
Antiplatelets	33(49.3)	2242(35.7)	0.03	0.31
Any antithrombotic	44(65.7)	5089(80.9)	0.003	0.002
Other medical therapy				
ACE-I	21(53.8)	1284(38.3)	0.05	0.04
Beta-blocker	16(41.0)	1602(47.8)	0.43	0.77
Digoxin	10(25.6)	958(28.6)	0.86	0.51
Diuretic	22(56.4)	1431(42.7)	0.10	0.65
Antiarrhythmic agent	12(29.3)	1914(49.0)	0.01	0.03
Calcium channel blocker	4(28.6)	289(18.4)	0.31	0.62
CHADS <sub>2</sub> Mean (s.d.)	2.7(1.3)	1.7(1.3)	<0.0001	0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASC Mean (s.d.)	4.4(1.6)	3.1(1.8)	<0.0001	0.023
HASBLED Mean (s.d.)	2.07(1.03)	1.5(1.08)	<0.0001	0.19

SD: standard deviation; AF: atrial fibrillation; ICD: implantable cardiac defibrillator; INR: international normalised ratio; CHADS<sub>2</sub> (1 point each for congestive heart failure, hypertension, age ≥75, and diabetes, and 2 points for previous stroke or thromboembolism); CHA<sub>2</sub>DS<sub>2</sub>-VASC (1 point for congestive heart failure, hypertension, diabetes, vascular disease, age 65-74, and female sex, and 2 points for previous stroke or thromboembolism and age ≥75); HAS-BLED (Hypertension, Abnormal renal and/or liver function, Stroke, Bleeding history or predisposition, Labile International Normalized Ratio (INR), Elderly (> 65 years))

**Table 2. Event rates (95% confidence interval) per 100 person years by prior history of falls**

	Prior history of falls n=76		No history of falls n=7080		
	Events	Event rate	Events	Event rate	P*
Ischaemic Stroke	9	1.18 (0.54,2.25)	353	0.50(0.45,0.55)	0.01
Ischaemic stroke/TE	12	1.58 (0.82,2.76)	533	0.75(0.68,0.83)	0.01
Haemorrhagic stroke	3	0.39(0.08,1.15)	98	0.14(0.11-0.17)	0.09
Bleeding	8	1.05 (0.45,2.07)	542	0.77(0.70,0.83)	0.38
All-cause mortality	20	2.63 (1.61,4.06)	827	1.17(1.07,1.27)	<0.0001

\*p-value for 2-sided chi-squared test

**Table 3. Event rates (95% confidence interval) per 100 person years by prior history of falls stratified by anticoagulation status**

	Prior history of falls					No history of falls				
	No VKA (n=59)		VKA (n=17)		p <sup>†</sup>	No VKA (n=3490)		VKA (n=3590)		p <sup>†</sup>
	Events	Event rate	Events	Event rate		Events	Event rate	Events	Event rate	
Ischaemic Stroke	3	0.51 (0.1,1.49)	5	2.94 (0.95,6.86)	0.08	151	0.43 (0.37,0.51)	170	0.47 (0.41,0.55)	0.30
Ischaemic Stroke/TE	6	1.02 (0.37,2.21)	5	2.94 (0.95,6.86)	0.12	218	0.62 (0.54,0.71)	267	0.74 (0.66,0.84)	0.70
Ischaemic Stroke/TE/All-cause mortality	18	3.05 (1.81,4.82)	8	4.71 (2.03,9.27)	0.39	518	1.47 (1.28,1.69)	509	1.42 (1.30,1.55)	0.88
Haemorrhagic stroke	2	0.34 (0.04,1.22)	1	0.59 (0.01,3.28)	0.99	34	0.10 (0.07,0.14)	59	0.16 (0.13,0.21)	0.14
Bleeding	4	0.68 (0.18,1.74)	4	2.35 (0.64,6.02)	0.09	172	0.49 (0.42,0.57)	323	0.9 (0.8,1.00)	0.10
All-cause mortality	14	2.37 (1.3,3.98)	5	2.94 (0.95,6.86)	0.99	339	0.97 (0.87,1.08)	376	1.05 (0.94,1.16)	0.79

<sup>†</sup>p-value for 2-sided chi-squared test comparing anticoagulated and non-anticoagulated individuals

**Table 4. Cox regression analyses for event rates in patients with prior history of falls.**

	<b>Ischaemic stroke and thromboembolism</b>	<b>Haemorrhagic stroke</b>	<b>Bleeding</b>	<b>All-cause mortality</b>
<b>Prior history of falls</b>	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
<b><i>Overall</i></b>				
Univariate	2.75(1.55-4.88); p=0.001	3.79(1.20-12.00);p=0.02	1.86(1.08-3.23);p=0.026	2.74(1.75-4.27);p<0.0001
Multivariate*	1.71(1.04-2.83); p=0.04	2.82(0.88-9.04);p=0.08	1.48(0.85-2.57); p=0.16	1.67(1.07-2.62);p=0.03
Multivariate**	1.71(1.04-2.83); p=0.04	2.92(0.91-9.37);p=0.07	1.49(0.86-2.58);p=0.16	1.68(1.07-2.62);p=0.02
<b><i>On OAC</i></b>				
Univariate	5.16(2.31-13.63);p<0.0001	4.76(0.66-34.51);p=0.12	3.79(1.41-10.19);p=0.008	4.36(1.80-10.57);p=0.001
Multivariate*	5.19(2.1-12.6);p<0.0001	4.20(0.58-30.48); p=0.16	3.32(1.23-8.91);p=0.02	3.69(1.52-8.95); p=0.04
Multivariate**	5.18(2.13-12.61);p<0.0001	4.36(0.60-31.83);p=0.15	3.70(1.38-9.97);p=0.01	3.91(1.61-9.51);p=0.003
<b><i>No OAC</i></b>				
Univariate	1.74(0.77-3.91);p=0.18	3.97(0.95-16.65);p=0.06	1.44(0.54-3.89);p=0.47	2.19(1.28-3.73);p=0.04
Multivariate*	0.88(0.38-2.01); p=0.75	3.26(0.75-14.15); p=0.12	1.08(0.40-2.95);p=0.88	1.28(0.74-2.21);p=0.37
Multivariate**	0.88(0.38-2.01);p=0.75	3.52(0.81-15.32); p=0.09	1.15(0.42-3.14);p=0.79	1.27(0.74-2.19);p=0.39

\*adjusted for CHA<sub>2</sub>DS<sub>2</sub>-VASc\*\*adjusted for CHA<sub>2</sub>DS<sub>2</sub>-VASc and HAS-BLED

**Clinical significance**

- Patients with non-valvular atrial fibrillation (NVAF) are often denied oral anticoagulation (OAC) due to falls risk.
- Among 7156 NVAF patients, prior history of falls/trauma was uncommon (1.1%), but independently increased risk of stroke/TE, bleeding and mortality, but not haemorrhagic stroke in the presence of anticoagulation.
- Prior history of falls may be a more clinically useful risk prognosticator than “risk of falls”.